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10/798,097	03/11/2004	Fredrik Nilsson	12578/46202	6060
26646 75500 09/23/2011 KENYON & KENYON LLP ONE BROADWAY NEW YORK, NY 10004			EXAMINER	
			STEELE, AMBER D	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Application No. Applicant(s) 10/798.097 NILSSON, FREDRIK Office Action Summary Examiner Art Unit Amber D. Steele 1654 -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --Period for Reply A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS. WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION. Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b). Status 1) Responsive to communication(s) filed on 09 August 2011. 2a) This action is FINAL. 2b) This action is non-final. 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11, 453 O.G. 213. Disposition of Claims 4) Claim(s) 1-17.19-21.24.26 and 27 is/are pending in the application. 4a) Of the above claim(s) 12.15.16.19 and 20 is/are withdrawn from consideration. Claim(s) _____ is/are allowed. 6) Claim(s) 1-11.13.14.17.21.24.26 and 27 is/are rejected.

7) Claim(s) _____ is/are objected to.

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DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 9, 2011 has been entered.

Status of the Claims

Claims 38-39, 44, and 47 were canceled in the amendment to the claims received on February 15, 2006.

Claims 22-23, 28-37, 40-43, 45-46, and 48-49 were canceled and claims 1-2, 7, 9, 10, 14, 21, and 24-27 were amended in the amendment to the claims received on August 25, 2006.

The amendment to the claims received on November 19, 2007 amended claim 1.

The amendment to the claims received on August 20, 2008 amended claims 1-6, 8, 14, and 26-27 and canceled claim 25.

The amendment to the claims received on February 19, 2009 changed the status identifiers only.

The amendment to the claims received on June 10, 2009 amended claim 1.

The amendment to the claims received on January 10, 2011 amended claim 1.

The amendment to the claims received on August 9, 2011 amended claims 1, 13, 14, 17 and canceled claim 18.

Claims 1-17, 19-21, 24, and 26-27 are currently pending.

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Claims 1-11, 13-14, 17, 21, 24, and 26-27 are currently under consideration.

Election/Restrictions

Applicant elected, with traverse, antibody as the species of binding molecule, C-terminal motif as the species of motif, and at least 10% as the species of capture in the reply filed on February 15, 2006. Claims 12, 15-16, and 19-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected species, there being no allowable generic or linking claim.

Priority

The present application claims priority to U.S. provisional application 60/454,229 filed March 12, 2003.

New Objections

Claim Objections

Claims 1-11, 13, 14, 17, 21, 24, 26, and 27 are objected to because of the following informalities: for consistency among the claims, "a specific antibody" of claim 1, line 10 should read "a specific antibody or fragment thereof" or "specific antibodies or fragments thereof", "antibody" of claim 13, lines 2, 4, and 5; claim 14, line 2; claim 17, line 2 should read "antibodies or fragments thereof" or "antibody or fragment thereof" (plural or singular where appropriate), "peptides" of claim 14, line 3 should read "proteins or peptides", and "peptides, or protein or peptide fragments" of claim 21, line 2 and claim 24, line 2 should read "proteins, peptides, protein fragments, or peptide fragments". Appropriate correction is required. Applicant is respectfully requested to carefully review the claims for consistency of claim language including withdrawn claims (e.g. see duplicate "or" in "proteins, peptides, or protein fragments

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or peptide fragments", each of the heterogeneous classes – each class is not heterogeneous – rather the collection of classes is heterogeneous, etc.).

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 13, 14, 17, 21, 24, 26, and 27 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. Applicants have not provided support for the amendments received on August 9, 2011 particularly for the amendments requiring "all" proteins, peptides, protein fragments, or peptide fragments to be characterized and "those proteins, peptides, protein fragments, or peptide fragments binding to a specific antibody represent a heterogeneous class".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 13, 14, 17, 21, 24, 26, and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to

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determine the scope of the presently claimed invention. The phrase "wherein the characterization is conducted using mass spectrometry" is indefinite. Method steps should be recited as positive. active method steps. In addition, a question as to the limiting effect of the language in a claim is raised when "wherein" clauses are utilized. Please refer to MPEP § 2173.05(a) and § 2111.04. Furthermore, the fragmented, performed, derived, used, etc. of present claims 3, 4, 5, 6, and 26 should be written as positive, active method steps. All "using" or "used" limitations should be altered to "utilizing", etc. (see claims 1, 5, and 26). Applicants are also respectfully requested to carefully review independent claim 1 regarding the various "wherein" clauses and to alter the claim language to incorporate positive, active method steps where necessary. Furthermore, the claim limitation "those proteins, peptides, protein fragments, or peptide fragments binding to a specific antibody represent a heterogeneous class" is considered indefinite because the other limitations of method step (a) of claim 1 would lead one of skill in the art to believe that a single class is not heterogeneous, a single antibody would bind a relatively homogeneous group of proteins, peptides, protein fragments, or peptide fragments (i.e. antibody would bind to a specific motif common to all proteins, peptides, protein fragments, or peptide fragments that bind to the specific antibody). Moreover, it is not clear how "more than one protein, peptide, protein fragment, or peptide fragment" can bind to "each defined location on the array" (i.e. more than one protein, peptide, protein fragment, or peptide fragment binds to a single location on the array). Are the single locations (e.g. spots, etc.) duplicated, is a certain size required, etc. Does the claim require that more than one protein, peptide, protein fragment, or peptide fragment binds to a single location on the array or is this simply a functional limitation regarding the binding characteristics of the heterogeneous sample, etc.?

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Altered Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior at are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-11, 13-14, 17, 21, 24, and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Minden et al. WO 02/086081 A2 (filing date April 22, 2002), Nelson et al. U.S. Patent 6,887,713 (effective filing date of March 11, 2000), and Kumar U.S. Patent Application Publication 2002/0110835 published August 15, 2002.

For present claim 1, Minden et al. teach methods of identifying a protein via assigning (i.e. separating) binding reagents to designated locations on an array, detecting the binding patterns, and comparing the binding pattern to a reference set (i.e. characterizing; please refer to the abstract, paragraphs [0005-0012], [0028-0032], [0035-0044], [0072-0074], [0077], [00117], Figures 1-11, and Table 1). In addition, Minden et al. teach that the molecular weight or mass of the binding reagents can be determined and that spectrometry can be utilized (please refer to paragraphs [0003-0004], [0030], [0036], [0048]; Figures 7-9). Furthermore, Minden et al. teach that more than one protein can have the same epitope thus the common epitopes (i.e. more than one) would bind to the same defined location (please refer to Figures 4A-4C and 5 and paragraphs 89-96). In addition, Minden et al. teach that the binding reagents can be antibodies (please refer to paragraphs [0029], [0056-0061], [0072]). Minden et al. discuss utilizing mass spectrometry in methods of identifying proteins (i.e. utilizing mass spectrometry in both

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homogenous and heterogeneous methods; paragraphs 3-4 and 136). Furthermore, Minden et al. teach heterogeneous protein mixtures including proteolytic cleavage of proteins (please refer to paragraphs 29-35). Moreover, Minden et al. teach that the protein mixture can be all of the proteins in a given organism, proteome, organ, tissue, cell, organelle, or sub-cellular localization (see paragraph 35) and thus all of the proteins are not necessarily known.

For present claim 2, Minden et al. teach that the total protein content of a cell or tissue can be utilized as the protein mixture (please refer to paragraphs [0035], [0066]).

For present claims 3-6, Minden et al. teach that the protein mixture can be fragmented with various chemical or enzymatic methods including trypsin (please refer to paragraph [0037-0039], [0066], [00105], [00107], and Table 1).

For present claims 7-8 and 11, Minden et al. teach that trypsin cleavage forms a peptide or epitope (i.e. motif) with C-terminal lysine or arginine residues (please refer to Table 1 and paragraphs [0041-0045], [0049], [0054], [0063]).

For present claims 9-10, Minden et al. teach that the peptides or epitopes (i.e. motifs) can be at least three amino acids in length and can have at least two variable amino acids (please refer to paragraphs [0029], [0032], [0040-0046], [0054], [00113-00116]).

For present claim 13, Minden et al. teach that arrays can have different binding molecules at spatially addressable locations which bind to different binding reagents (please refer to paragraphs [0005], [0008], [0012], [0028], [0040]).

For present claim 14, Minden et al. teach that the protein mixture may comprise all (i.e. at least 10% of the peptides) of the proteins and that the epitopes cover the binding mixture (please refer to paragraph [0035], [0040]).

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For present claim 17, Minden et al. teach that the array can have 2-100 different proteins (please refer to paragraphs [0047], [0073-0074]).

For present claim 21, Minden et al. teach that the proteins are compared to a reference set (i.e. characterizing; please refer to paragraphs [0005], [0028-0031], [0040]).

For present claim 27, Minden et al. teach that various binding reagents can be compared to a reference set or to other binding reagents (please refer to paragraphs [0005], [0030-0031, [0040], [0053]).

However, Minden et al. does not specifically teach determining the abundance of the proteins by the use of desorption mass spectrometry or collision induced dissociation mass spectrometry.

For present claims 1, 24, and 26, Nelson et al. teach analyzing complex biological mixtures utilizing "lab-on-a-chip" (i.e. chip-based microarrays) and MALDI-TOF (i.e. combination of both desorption mass spectrometry and collision induced dissociation mass spectrometry) wherein the proteins are quantified (i.e. abundance), internal reference standards are utilized, and determining the amount (i.e. abundance) of the proteins (please refer to the entire specification particularly the abstract; Figures 1, 4, 7, 8a-c, and 10a-c; column 1, lines 54-67; columns 2-3; column 4, lines 1-30; column 6, lines 52-67; column 8, lines 19-64; column 9, lines 13-35; columns 10-11 and 14-15; column 16, lines 1-10; column 17, lines 30-45). Nelson et al. discuss utilizing mass spectrometry in methods of identifying proteins (i.e. utilizing mass spectrometry in both homogenous and heterogeneous methods; columns 9-10). Nelson et al. teach utilizing MALDI-TOF for quantitative analysis including analysis of proteins from biofluids, heterogeneous analyte systems, sample comprising point mutations, etc. (i.e.

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heterogeneous sample; see column 2, lines 42-46; paragraph spanning columns 3-4; columns 5, 8-11, 15-16; Examples 3 and 6).

While Minden et al. discusses utilizing antibodies as binding reagents and immobilization of binding reagents onto arrays or substrates (see paragraphs 28 and 29), the specific examples provided by Minden et al. have the proteins, peptides, etc. immobilized on the array.

For present claims 1, 24, 26, and 27, Kumar teaches proteomic analysis comprising providing a substrate comprising distinct spots or deposits including an array of antibodies, exposing the antibody array to a sample containing proteins to allow capture of specific proteins, and subsequently interfacing the substrate (i.e. antibody array with bound proteins) with a MALDI-TOF instrument for identification of the proteins captured on the substrate/antibody array (please refer to the entire specification particularly abstract; paragraphs 27, 33, 37; Example 1).

The claims would have been obvious because the substitution of one known element (i.e. mass spectrometry providing mass information only as taught by Minden et al.) for another (i.e. mass spectrometry providing both mass and abundance information; MALDI-TOF as taught by Nelson et al. and Kumar) would have yielded predictable results (i.e. analysis of both mass and abundance at the same time) to one of ordinary skill in the art at the time of the invention and/or (b) the claim would have been obvious because a particular known technique (i.e. MALDI-TOF utilized to determine mass and abundance of proteins bound to antibody arrays) was recognized as part of the ordinary capabilities of one skilled in the art. See KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 1741 (2007).

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Therefore, the teaching of Minden et al., Nelson et al., and Kumar render the presently claimed invention *prima facie* obvious.

Claims 1-11, 13-14, 17, 21, 24, and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Minden et al. WO 02/086081 A2 (filing date April 22, 2002), Barry et al. WO 0225287 (filed September 19, 2001), and Kumar U.S. Patent Application Publication 2002/0110835 published August 15, 2002.

For present claim 1, Minden et al. teach methods of identifying a protein via assigning (i.e. separating) binding reagents to designated locations on an array, detecting the binding patterns, and comparing the binding pattern to a reference set (i.e. characterizing; please refer to the abstract, paragraphs [0005-0012], [0028-0032], [0035-0044], [0072-0074], [0077], [00117], Figures 1-11, and Table 1). In addition, Minden et al. teach that the molecular weight or mass of the binding reagents can be determined and that spectrometry can be utilized (please refer to paragraphs [0003-0004], [0030], [0036], [0048]; Figures 7-9). Furthermore, Minden et al. teach that more than one protein can have the same epitope thus the common epitopes (i.e. more than one) would bind to the same defined location (please refer to Figures 4A-4C and 5 and paragraphs 89-96). In addition, Minden et al. teach that the binding reagents can be antibodies (please refer to paragraphs [0029], [0056-0061], [0072]). Minden et al. discuss utilizing mass spectrometry in methods of identifying proteins (i.e. utilizing mass spectrometry in both homogenous and heterogeneous methods; paragraphs 3-4 and 136). Furthermore, Minden et al. teach heterogeneous protein mixtures including proteolytic cleavage of proteins (please refer to paragraphs 29-35), Moreover, Minden et al, teach that the protein mixture can be all of the

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proteins in a given organism, proteome, organ, tissue, cell, organelle, or sub-cellular localization (see paragraph 35) and thus all of the proteins are not necessarily known.

For present claim 2, Minden et al. teach that the total protein content of a cell or tissue can be utilized as the protein mixture (please refer to paragraphs [0035], [0066]).

For present claims 3-6, Minden et al. teach that the protein mixture can be fragmented with various chemical or enzymatic methods including trypsin (please refer to paragraph [0037-0039], [0066], [00105], [00107], and Table 1).

For present claims 7-8 and 11, Minden et al. teach that trypsin cleavage forms a peptide or epitope (i.e. motif) with C-terminal lysine or arginine residues (please refer to Table 1 and paragraphs [0041-0045], [0049], [0054], [0063]).

For present claims 9-10, Minden et al. teach that the peptides or epitopes (i.e. motifs) can be at least three amino acids in length and can have at least two variable amino acids (please refer to paragraphs [0029], [0032], [0040-0046], [0054], [00113-00116]).

For present claim 13, Minden et al. teach that arrays can have different binding molecules at spatially addressable locations which bind to different binding reagents (please refer to paragraphs [0005], [0008], [0012], [0028], [0040]).

For present claim 14, Minden et al. teach that the protein mixture may comprise all (i.e. at least 10% of the peptides) of the proteins and that the epitopes cover the binding mixture (please refer to paragraph [0035], [0040]).

For present claim 17, Minden et al. teach that the array can have 2-100 different proteins (please refer to paragraphs [0047], [0073-0074]).

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For present claim 21, Minden et al. teach that the proteins are compared to a reference set (i.e., characterizing; please refer to paragraphs [0005], [0028-0031], [0040]).

For present claim 27, Minden et al. teach that various binding reagents can be compared to a reference set or to other binding reagents (please refer to paragraphs [0005], [0030-0031, [0040], [0053]).

However, Minden et al. does not specifically teach determining the abundance of the proteins by the use of desorption mass spectrometry or collision induced dissociation mass spectrometry.

Barry et al. teach methods of determining the binding and mass of trypsin digested proteins including antibodies from a cell including phage or tissue sample immobilized on an array (please refer to the abstract, pages 2-6, 21-30, Figures 3-6 and 8-10, Examples 2-3).

For present claim 1, Barry et al. teach determining the abundance of proteins via MALDI-TOF (i.e. mass; please refer to pages 5-6, page 32, lines 25-33, page 33, lines 21-37, pages 34-35, Figures 3-6 and 8-10, Examples 2-3). Barry et al. discuss utilizing mass spectrometry in methods of identifying proteins (i.e. utilizing mass spectrometry in both homogenous and heterogeneous methods; pages 33-35). Barry et al. teach quantitative or semi-quantitative analysis via MALDI-TOF wherein the sample can include body fluid, tissue, or cell (i.e. heterogeneous; please refer to pages 3, 9, 21, 28, 32-34, 45-46).

For present claim 24, Barry et al. teach MALDI-TOF (i.e. matrix assisted laser desorption ionization-time of flight) mass spectrometry (i.e. combination of both desorption mass spectrometry and collision induced dissociation mass spectrometry or CID; page 35, line 7;

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please refer to pages 5-6, page 32, lines 25-33, page 33, lines 21-37, pages 34-35, Figures 3-6 and 8-10, Examples 2-3).

For present claim 26, Barry et al. teach determining the abundance of the protein via MALDI-TOF including proteins from any given starting material (i.e. unfragmented parent protein; please refer to page 3, lines 28-30; pages 5-6; page 32, lines 25-33; page 33, lines 21-37; pages 34-35; Figures 3-6 and 8-10, Examples 2-3).

While Minden et al. discusses utilizing antibodies as binding reagents and immobilization of binding reagents onto arrays or substrates (see paragraphs 28 and 29), the specific examples provided by Minden et al. have the proteins, peptides, etc. immobilized on the array.

For present claims 1, 24, 26, and 27, Kumar teaches proteomic analysis comprising providing a substrate comprising distinct spots or deposits including an array of antibodies, exposing the antibody array to a sample containing proteins to allow capture of specific proteins, and subsequently interfacing the substrate (i.e. antibody array with bound proteins) with a MALDI-TOF instrument for identification of the proteins captured on the substrate/antibody array (please refer to the entire specification particularly abstract; paragraphs 27, 33, 37; Example 1).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of identifying proteins taught by Minden et al. with the MALDI-TOF analysis taught by Barry et al.

One having ordinary skill in the art would have been motivated to do this because Barry et al. teach that the use of mass spectrometry and MALDI-TOF provide semi-quantitative and quantitative results for protein microarrays (please refer to page 1, lines 20-26 and 34-37; page 2, lines 1-24; page 3, lines 5-30; Examples 2-3).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the method of identifying proteins taught by Minden et al, with the MALDI-TOF analysis taught by Barry et al. because of the examples provided by Barry et al. show that trypsin digested antibody arrays can be quantitated via MALDI-TOF (please refer to Examples 2-3).

The claims would have been obvious because the substitution of one known element (i.e. mass spectrometry providing mass information only as taught by Minden et al.) for another (i.e. mass spectrometry providing both mass and abundance information; MALDI-TOF as taught by Barry et al. and Kumar) would have yielded predictable results (i.e. analysis of both mass and abundance at the same time) to one of ordinary skill in the art at the time of the invention and/or (b) the claim would have been obvious because a particular known technique (i.e. MALDI-TOF utilized to determine mass and abundance of proteins bound to antibody arrays) was recognized as part of the ordinary capabilities of one skilled in the art. See KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 1741 (2007).

Therefore, the modification of the method of identifying proteins taught by Minden et al. with the MALDI-TOF analysis taught by Barry et al. and Kumar render the instant claims prima facie obvious.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Duffy U.S. Patent Application Publication 2002/0028463 published March 7, 2002.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/ Primary Examiner, Art Unit 1654